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## Respiratory Disease Rates and Pulmonary Function in Children Associated with NO<sub>2</sub> Exposure<sup>1-4</sup>

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### SUMMARY

As part of a long-range, prospective study of the health effects of air pollution, approximately 8,000 children from 6 yrs to 10 yrs of age from 6 communities had questionnaires completed by their parents and had simple spirometry performed in school. Comparisons were made between children living in homes with gas stoves and those living in homes with electric stoves. Children from households with gas stoves had a greater history of respiratory illness before age 2 (average difference, 32.5/1,000 children) and small but significantly lower levels of FEV<sub>1</sub> and FVC corrected for height (average difference, 16 ml and 18 ml, respectively). These findings were not explained by differences in social class or by parental smoking habits. Measurements taken in the homes for 24-h periods showed that NO<sub>2</sub> levels were 4 to 7 times higher in homes with gas stoves than in homes with electric stoves. However, these 24-h measurements were generally well below the current federal 24-h outdoor standard of 100 µg/m<sup>3</sup>. Short-term peak exposures, which were in excess of 1,100 µg/m<sup>3</sup>, regularly occurred in kitchens. Further work will be required to determine the importance of these short-term peaks in explaining the effects noted.

### Introduction

There is little doubt that NO<sub>2</sub> at high concentration is associated with acute pulmonary edema and death. Silo filler's disease in which farmers are exposed to concentrations of NO<sub>2</sub> in excess of 200 ppm (376,000 µg/m<sup>3</sup>) with a resultant occurrence of acute pulmonary disease and occasionally death was described in the 1950s (1). Farmers surviving such exposures can develop pulmonary fibrosis.

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Recently, concern over the effects of indoor exposure to lesser concentrations of NO<sub>2</sub>, both repeated short-term peak exposure and continuous low exposure, has led to studies of children (2) and housewives (3) but with inconsistent results. Melia and co-workers (2) from Great Britain reported higher rates of lower respiratory disease in school children living in households with gas cooking stoves than in those living in households with electric stoves. These differences in rates could not be explained by social class or differences in household size. However, this study did not take into account the smoking habits of the parents of these children. Subsequently, Melia and co-workers (4) found that households with gas cooking stoves had 7 times higher concentrations of NO<sub>2</sub> in the kitchen than did matched households with electric cooking devices. Similar studies in the United States found concentrations

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of NO<sub>x</sub> 4 times greater in kitchens of households with gas stoves than in those with electric stoves (5). The NO<sub>x</sub> appears to be produced by the oxidation of NO when natural gas as a fuel for cooking is burned in the atmosphere. The conversion is rapid, and the NO<sub>x</sub> spreads quickly throughout the house. In contrast to the Melia study of children (2), a study of adult women living and working in households with gas stoves compared with those living and working in households with electric stoves did not show increased respiratory disease rates (3).

The results reported here were obtained as part of a long-range prospective study on the health effects of exposure to ambient levels of pollutants resulting from the burning of fossil fuels. In this study, adults between the ages of 25 and 74, selected at random from 6 communities in the eastern United States, are seen every 3 years, and school children (initially seen in grades 1 and 2) are seen annually. This report is based on the initial measurements of pulmonary function and information on respiratory diseases obtained in the children only in the 6 cities and relates these measurements to the potential indoor exposure that these children have received.

#### Methods

**Study design.** A total of 9,280 children participated in the initial surveys. These children represented 12 separate cohorts from 6 cities. Two cities were surveyed for 3 years, and a new group of first-grade school children was added each year. Thus, these cities provided 6 cohorts. Two cities were surveyed for 2 years giving 4 more cohorts, and 2 cities were surveyed once. In all the cohorts, more than 95 % of the children eligible because of their school grade were studied.

Information about the children's exposure was obtained from a questionnaire, completed by their parents, on the type of home-cooking device and home-heating fuel, the presence or absence of air conditioning, and the presence or absence of adult smokers living in the household, as well as requesting permission to perform lung function tests on the children in the schools.

Forced expiratory measurements were performed using a water-filled low-inertia recording spirometer. The children did not wear nose clips and performed the task in a sitting position, but with free movement possible. Each child had a minimum of 5 and a maximum of 8 attempts in an effort to obtain at least 3 acceptable tracings. Forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV<sub>1</sub>) were read from each tracing. Values were corrected to body temperature and pressure saturated with water vapor (BTPS) and summarized as the mean of the 3 best efforts that were within 170 ml of each other. Standing height in stockinged feet and weight were recorded for each child.

There were 8,866 children (95.5 % of the total seen) who were between 6 yrs and 10 yrs of age at the time of their initial survey, but the sample was reduced to 8,120 children by limiting the analyses to white children.

For each child included in the study, the lung function predicted for his or her height was computed from a regression equation determined by using the children studied in the third year of follow-up from 2 of the cities. These children, who were all within the 5 to 95 percentiles for their height corrected for age, were chosen for the standard as they provided sufficient numbers at each year of age between 6 yrs and 10 yrs (6). The difference between the observed lung function and the predicted value was obtained. These residuals were analyzed using standard analysis of variance techniques.

The reported disease rates were analyzed using log-linear models. By this means it was possible to determine significant interactions between disease, age, sex, cohort, city, and home variables. Adjusted rates were computed based on models that included the significant interactions (7).

Information regarding the differences in air quality associated with different cooking devices was obtained by setting up indoor-outdoor monitors in selected households. These households were not necessarily the homes of children in the study, but were selected to be representative of the kinds of living patterns found in each community. The homes were sampled every sixth day for 24 h, and the same time period in each city, May 1977 through April 1978, was used in all analyses. Measurements were carried out by a household sampling unit, which was placed in an "activity room," a room specifically defined as not being the kitchen or bedroom. Mass respirable particulates (mass median diameter of 3.5  $\mu\text{m}$ ) were collected on millipore filters (8), and NO<sub>x</sub> was collected by a bubbler technique and measured by the EPA Reference Method, a modified sodium arsenite method (9).

The data on air pollution levels were first adjusted to take into account missing values using a linear model for day of observation and site. The influence of home variables was determined by analysis of variance, with appropriate adjustment of the residual degrees of freedom. In one household, instantaneous peak levels of NO<sub>x</sub> were monitored in the kitchen within 3 feet of a gas stove using a chemiluminescence monitor and a continuous recording.

#### Results

**Assessment of exposure to NO<sub>x</sub>.** About half of the homes in all 6 cities had gas cooking stoves, and about half had electric cooking stoves. (Six % of the homes used some other form of cooking device, alone or in conjunction with gas and/or electricity [1.9 %], or else the type of cooking device was not reported [4.1 %].) There were, however, considerable differences between cities (figure 1). The distribution of the children by home cooking device ranged from a high of 82.2 % gas cooking

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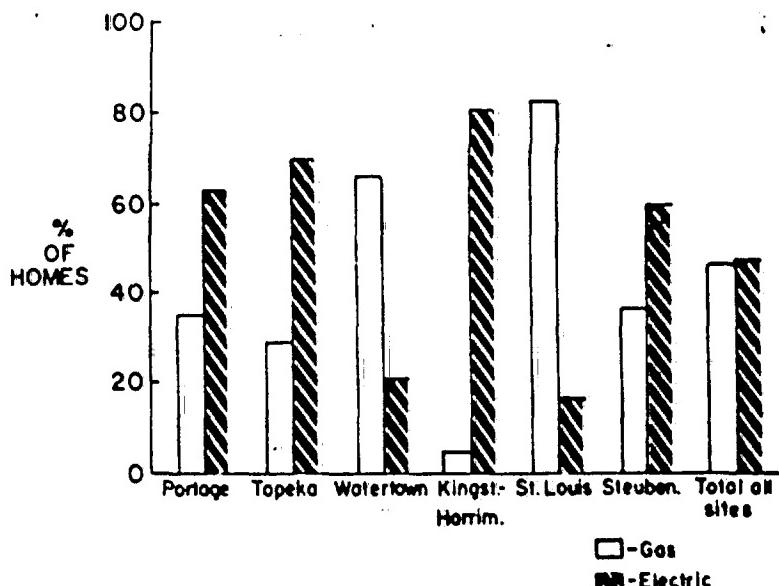


Fig. 1. Percentage of homes with gas or electric stoves, by cities.

stoves in St. Louis to a low of 4.6 % in Kingston-Harriman (figure 1).

Although the number of homes where air quality measurements were made is not large, ranging between 5 and 11 for different cities, the number of 24-h periods for which matched indoor and outdoor data are available is several hundred (table 1). The homes were divided between gas and electric cooking devices, except for Kingston-Harriman where no homes with gas stoves were studied. The results show a gradient of NO<sub>2</sub> levels in homes with electric stoves that reflect outdoor sources of NO<sub>2</sub>. High concentrations in Watertown were presumed to be caused by the proximity of homes, and therefore the monitors, to automobile traffic. A substantial increase in NO<sub>2</sub> levels in homes with gas stoves, except for Steubenville, reflects the addition of indoor sources to the outdoor level of NO<sub>2</sub>. These are 24-h integrated averages collected in an "activity room," but not in the kitchen. In some cities the daily 24-h levels encountered in some households with gas stoves exceeded the federal standard for the annual average of the 24-h NO<sub>2</sub> levels (100 µg/m<sup>3</sup>). Such levels for integrated 24-h values indicated that peak exposures must be substantially higher. This was confirmed in 1 household in which instantaneous monitoring in the kitchen produced peak levels over 1,100 µg/m<sup>3</sup> for short periods of time when the oven was in use and peaks over 500 µg/m<sup>3</sup> when a single gas burner was on (figure 2).

**Health data.** Two sets of data on the children's

health were available: data on previous illnesses reported on questionnaires completed by parents, and data from the current pulmonary function tests. The responses to 3 questions about the previous health of the children were analyzed. The questions asked if there was a history of bronchitis diagnosed by a physician, a history of serious respiratory disease before age 2, and a history of a respiratory illness in the last year.

Both the responses to these questions and the pulmonary function measurements were tested for their relationship to several household variables: type of cooking device, nature of fuel used for heating, presence of adult smokers, presence of air conditioning, and socio-economic status of the family. Socio-economic status included both occupation and educational attainment of the parents.

The 3 reported disease rates were analyzed by fitting log-linear models (7). Two of the variables, type of home-heating fuel and air conditioning, were not related to the disease rates. The social class, parental smoking, and type of cooking stove variables had differing effects on the 3 diseases when each home variable was tested alone (table 2). As the risk factors themselves were interrelated, each disease was evaluated in another log-linear analysis that included these 3 home variables simultaneously. In this multivariate analysis, the effect of the type of cooking stove had a significant association with respiratory disease before age 2, but not with the other 2 reported dis-

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TABLE 1  
INDOOR AND OUTDOOR 24-H LEVELS OF NO<sub>x</sub> IN 6 U.S. CITIES  
(MAY 1977 TO APRIL 1978)

City	Home Cooking Units			Geometric Mean Level of NO <sub>x</sub> (µg/m <sup>3</sup> )				95 Percentile Measured Level of NO <sub>x</sub> (µg/m <sup>3</sup> )			
	Days (no.)	Elec. (no.)	Gas (no.)	Outdoor		Indoor		Outdoor		Indoor	
				Electric	Gas	Electric	Gas	Electric	Gas	Electric	Gas
Portage*	50	8	3	7.2 (1.95)†	5.9 (1.10)	3.6 (2.13)	14.7 (1.02)	31.8	25.4	17.8	39.3
Topeka	57	6	1	17.5 (1.25)	18.2 —	19.4 (1.26)	31.6 —	42.4	40.7	41.6	73.6
Kingston-Harriman	56	8	—	17.2 (1.25)	— —	10.9 (1.43)	— —	38.4	—	29.8	—
St. Louis	58	3	6	33.0 (1.17)	37.3 (1.14)	17.1 (2.01)	40.8 (1.42)	64.3	70.9	63.3	79.3
Steubenville	61	2	3	35.7 (1.00)	33.3 (1.35)	21.9 (2.59)	27.4 (2.24)	82.9	87.8	74.5	103.9
Watertown	59	2	5	49.1 (1.42)	49.2 (1.10)	41.43 (1.14)	54.3 (1.21)	101.6	106.3	95.2	118.3

\* Based on 10-month sample.

† Federal 24-h standard = 100 µg/m<sup>3</sup>.

† Numbers in parentheses are geometric standard deviations.

enves (table 3). Parental smoking, sex of the child, and city-cohort, but not age at the time of report, were all associated with respiratory disease before age 2 after other variables were taken into account. Disease rates adjusted for parental smoking, social class, and city-cohort resulted in a difference of 35/1,000 among males and 30/1,000 among females between children in homes with different cooking stoves. Lower rates were found in children of households with electric stoves for each sex in each city-cohort adjusted for parental smoking and social class (figure 3). The effects of parental smoking and city-cohort on respiratory disease before age 2 are not independent, but the

effect of the type of cooking stove appeared to be related to the other home variables.

To assess the effect of home factors on pulmonary function in these children, the difference between the expected and observed FVC and FEV<sub>1</sub> was calculated for each child. The effect of cohort (yr of study and city) and the same home variables on the residual pulmonary function were assessed by analysis of variance. Preliminary regression of lung function on socio-economic status showed no relationship. There was a significant effect ( $p < .01$ ) of cohort on both FEV<sub>1</sub> and FVC. Thus, from city to city and from year to year there were differences in the height-adjusted pulmonary

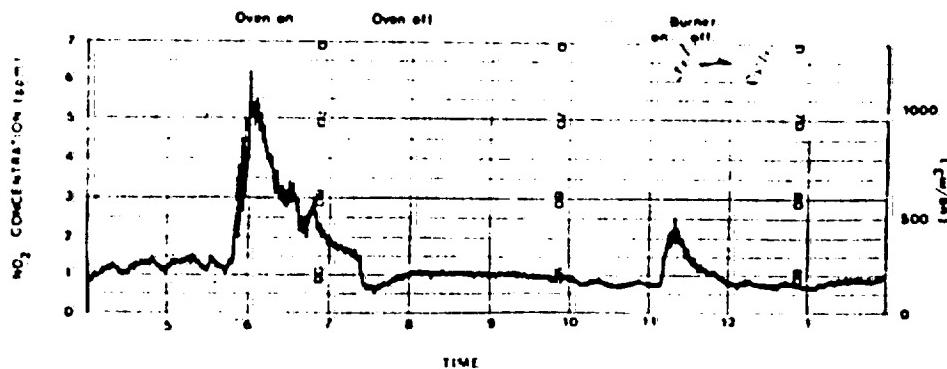


Fig. 2. Instantaneous monitoring of NO<sub>x</sub> in the kitchen 1 meter from gas stove. Numbers along the abscissa represent hr in the day through 1 A.M. No venting was used.

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TABLE 2  
SINGLE FACTOR ODD RATIOS (OR) AND 95% CONFIDENCE LIMITS (CL)  
FOR HOME VARIABLES AND REPORTED DISEASE RATES

	Social Class (Low/Hight)	Parental Smoking (Some/None)	Home Cooking (Gas/Electric)	
History of doctor-diagnosed bronchitis	OR CL	0.87 0.81-1.08	1.09 0.84-1.20	0.88 0.79-0.91
Serious respiratory illness before age 2	OR CL	1.13 1.01-1.26	1.32 1.12-1.57	1.12 1.00-1.26
Respiratory illness in the last year	OR CL	1.13 1.08-1.22	1.18 1.02-1.39	0.94 0.68-1.05

function levels in these children, after adjusting for city-cohort effects. There were no significant associations between the presence of air conditioning in the home and lung function measurements (table 4). Although the association between parental smoking and FVC was significant at the 5 % level, with an average range of 15 ml, the result was the opposite of that anticipated, and there was no association between FEV<sub>1</sub> and parental smoking. Home heating and FEV<sub>1</sub> residuals were also significantly associated at the 5 % level. The over-all means covered a 28-ml range and the ordering from low to high was oil, gas, electric.

Although FEV<sub>1</sub> residuals were affected by home heating fuels, the most consistent and significant finding was the lower levels of both FVC and FEV<sub>1</sub> in children whose homes had gas cooking stoves compared with those whose homes had electric stoves. The over-all effect of home cooking, after correcting for cohort effect, was 16 ml and 18 ml, respectively, for FEV<sub>1</sub> and FVC. This effect is apparent in almost all the cohorts. For FEV<sub>1</sub>, in 10 of 12 cohorts, the children in homes with gas stoves had lower function than children in homes with electric stoves (figure 4). For FVC, only 1 of the cohorts (St. Louis, first year), did not show lower levels of pulmonary function in children living in homes with gas stoves compared with those living in homes with electric stoves (figure 4). An unexpected finding in these data

was the low level of pulmonary function measured in Topeka, which is a city with generally lower levels of ambient pollution. In an attempt to investigate this finding, we tested the effect of different interviewers, we reread the spirometer tracings to test the effect of readers, and we compared the values obtained on each spirometer by month of study to test the possibility of a defective machine. None of these tests explained the lower pulmonary function values. In addition, the distribution of height for age of the children in Topeka did not differ significantly from the other cities. We were thus left with the observation that the pulmonary function measurements in the children in Topeka were lower than in other cities and must assume that it was a cohort effect needing further study.

#### Discussion

The significant associations found in this analysis were between home cooking stoves and both illness history and lung function. In addition, there was an association between parental smoking and disease history. The importance of these findings rests with the interpretations of these significant, albeit relatively small, changes. Sufficiently large groups are being studied to observe minor differences between them. The size of the differences found was consistent with the anticipated magni-

TABLE 3  
VALUES OF G<sup>2</sup> FOR SPECIFIED DISEASE RATES FOR EACH HOME VARIABLE  
AFTER ADJUSTING FOR THE OTHER TWO HOME VARIABLES

	Social Class G <sup>2</sup>	P	Parental Smoking G <sup>2</sup>	P	Home Cooking G <sup>2</sup>	P
History of doctor-diagnosed bronchitis	0.70	NS	1.10	NS	1.00	NS
Serious respiratory illness before age 2	4.12	<.05	10.21	<.01	6.70	<.01
Respiratory illness in the last year	2.12	NS	4.38	<.05	0.14	NS

\* G<sup>2</sup> is a likelihood statistic derived from the log-linear analyses and is distributed, in each case, like a chi-square with 1 degree of freedom.

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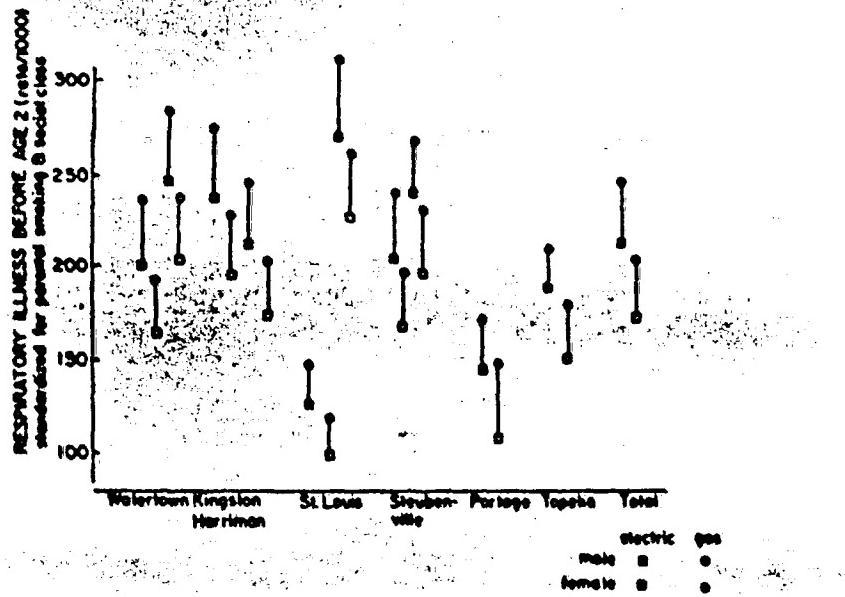


Fig. 3. Respiratory illness before age 2 standardized for parental smoking and social class by cohorts in children 6 to 10 yrs old. Males and females separately by cohort and gas or electric stoves.

tude of effect of environmental agents (11), and the home measurements of air quality are supportive.

The evidence that homes with gas cooking stoves have higher levels of NO<sub>x</sub> than similar homes with electric stoves has been demonstrated a number of times (4, 5), and peak levels measured over gas stoves have on occasion been re-

ported to reach approximately 1 ppm (1,880  $\mu\text{g}/\text{m}^3$ ) for periods of 10 to 15 min. This was confirmed in 1 household during continuous monitoring. Similarly we know from both our own investigation and from the studies of Hinds and associates (12) that the mass respirable particulate loads in households with smokers can be several-fold higher than in nonsmoking households.

TABLE 4  
ANALYSIS OF VARIANCE OF CHILDREN'S LUNG FUNCTION FOR HOME VARIABLES  
(CITY-COHORT ADJUSTED)\*

Home Variable	Children (no.)	Lung Function Residuals			
		FEV, (liter)	F Ratio	FVC (liter)	F Ratio
Cooking fuel	6,803	—	—	—	—
gas	3,274	-.008	8.11†	-.009	7.94†
electric	3,529	+.008		+.009	
Home fuel	6,734	—	—	—	—
oil	1,419	-.011		-.005	
gas	4,432	+.001	3.26†	-.005	0.76
electric	883	+.017		+.010	
Air conditioning	7,126	—	—	—	—
none	2,855	-.001		-.002	
partial	2,363	+.003	0.81	+.006	1.22
central	1,908	-.003		-.004	
Parentalismoking	6,842	—	—	—	—
none	1,724	-.001	.03	-.011	0.28†
some	4,118	+.000		+.004	

\* See text for definition of different cohorts. Largest cohort-home variable interaction terms gave F ratio of 1.3, not significant.

† p < .01.

‡ p < .05.

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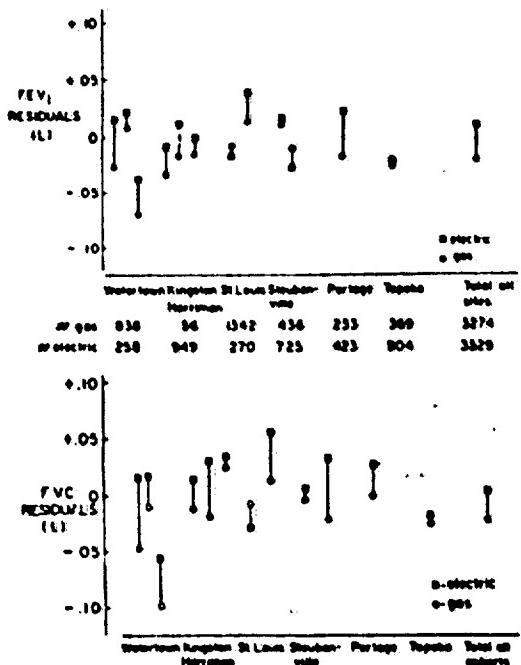


Fig. 4. Forced expiratory volume in 1 s and forced vital capacity residuals by cohort and gas and electric stoves in children 6 to 10 yrs old. (Numbers under the FEV<sub>1</sub> values are the same for FVC values.)

Other factors affecting the association between the disease and either the presence of gas stoves or smoking in the household seem to have been excluded (e.g., socio-economic status, presence of air conditioning, and the type of heating fuel).

In considering the importance of these findings, a number of potential sources of bias must be evaluated. The questionnaire information on disease rates for an individual child depends on the recall ability of the parents, and it may be biased by the present status of the child. The responses also may be biased by the parents' lack of knowledge. No attempt was made to have doctor confirmation of diagnosed disease confirmed independently. It seems unlikely, however, that any biases introduced by these means would be related to the type of home cooking stove consistently for each city and each cohort.

The good response rate, and the sampling plan that ensures that all potentially available children are seen means that the samples are representative of the cities.

The pulmonary function data are potentially subject to different sources of bias than the questionnaire data. These include possible interviewer bias, malfunctioning machine, and biased reading of the spirometer tracing. All these sources of bias have been looked for and have not been found. In

any case, neither the field screeners nor the readers were aware of the individual child's home environment when the spirometry was performed or when the tracings were read. Thus, we cannot attribute any bias to association with home variables.

Essentially, the interpretation of the pulmonary function finding relates to the sensitivity of the measurement and the biologic expectation of the magnitude of anticipated effect in a group of children between 6 yrs and 10 yrs of age. We used FEV<sub>1</sub> as a measure of air flow obstruction in these children, not because we believed it to be the best measure of early obstruction, but because our plan is to follow these children over several years. After several years they will be at a point at which a stable estimate of change in pulmonary function can be related to our understanding of the development of adult obstructive airways disease. In these children, many of whom can empty their entire FVC in less than 2 s, the FEV<sub>1</sub> does not measure obstruction as much as it measures FVC. Thus, it is reassuring to find similar changes in both measures when trying to understand the significance of any given finding.

Our understanding of the biology of lung growth and the nature of the onset of obstructive lung disease in adult life lead us to believe that only minor difference in the rate of functioning lung growth in young children could lead to these children not reaching their full adult lung size. (We are using FVC as a crude indicator of lung size recognizing that the TLC includes not only FVC but also the residual volume, which is not being measured in these field studies.) We do not know whether failure to reach full adult lung size is related to the subsequent susceptibility of developing obstructive lung disease, but it is not an untenable hypothesis that those persons with minor impairment of total lung growth are more susceptible to rapid decline in pulmonary function in adult life (13).

These results differed from those reported in the literature to date only in modest ways. The findings of Melia and co-workers (2) regarding lower respiratory tract illness rates in children whose homes have gas stoves were similar. That study was criticized because it did not have smoking data. In this study the adjustment of rates of illness before age 2 for smoking led to a clear association with gas cooking devices; however, the adjustment of the other 2 historical disease indicators reduced the associations found. The study of Keller and associates (14) of both adults and children in a selected sample of households suggest no association of gas stoves with respi-

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tory disease rates. This study measured incidence of acute respiratory disease over the course of 1 year; but the number of children studied was quite small and clearly did not represent a general population. Bouhuys and co-workers (15) did study population-based samples of children and adults, but out of the 7,000 persons studied only 165 children between the ages of 7 yrs and 14 yrs were included from the 2 communities under investigation (16). Thus, the fact that they were unable to find an association with home cooking devices may be attributed to the small number studied.

Tager and associates (17), using a different indicator of airways obstruction (mid-maximum expiratory flow), found an association between the pulmonary function levels in children and the number of smokers in the household. No such association using FEV<sub>1</sub> was found in this study. This may mean that the airways obstruction measurement was insensitive.

Further follow-up of these cohorts are underway. Because these data deal with retrospective information, the initial findings reported here need replication to ensure that some subtle bias or alternative explanation for the findings has not been overlooked. If the relative position of these children's lung sizes changes on repeated assessment, it will be important to assess the factors that influence the change. These factors may include changes in ambient pollution (outdoor levels) or changes in personal pollution (indoor exposures and cigarette smoking). In addition, other personal factors such as frequency of respiratory infections, familial history of disease, or other recognized potential risk factors for developing chronic obstructive respiratory disease not discussed in this report will need to be considered.

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